



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) Publication number: 0 484 112 A2

(12)

EUROPEAN PATENT APPLICATION

(21) Application number: 91309994.1

(31) Int. CL⁶: A61K 33/00, A61K 31/20,
A61K 31/19, A61K 31/505,
A61K 33/14, A61K 47/20,
// (A61K33/00, 31:17, 31:60),
(A61K31/60, 31:19, 31:20,
31:505), (A61K33/14, 31:17,
31:60)

(22) Date of filing: 30.10.91

(30) Priority: 31.10.90 GB 8023701

(72) Inventor: Horrobin, David Frederick
5n Maple Lodge, Lythe Hill Park
Haslemere, Surrey (GB)

(43) Date of publication of application:
06.05.92 Bulletin 92/19

(74) Representative: Cockbain, Julian et al
Frank B. Dohm & Co. Imperial House 15-19,
Kingsway
London WC2B 6UZ (GB)

(34) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LU NL SE

(71) Applicant: EFAMOL HOLDINGS PLC
Efamol House Woodbridge Meadows
Guildford Surrey GU1 1BA (GB)

(54) Use of lithium in the treatment or prophylaxis of Molluscum contagiosum.

(57) The present invention provides use of a physiologically acceptable lithium compound in the manufacture of a medicament for use in the treatment and/or prophylaxis of Molluscum Contagiosum. It also extends to pharmaceutical compositions comprising a physiologically acceptable lithium compound together with at least one keratolytic and/or skin penetration assisting agent and at least one pharmaceutically acceptable carrier or excipient.

EP 0 484 112 A2

Jouve, 18, rue Saint-Denis, 75001 PARIS

BEST AVAILABLE COPY

The present invention relates to the treatment of skin disorders and in particular to a new medical use for lithium in the treatment of Molluscum Contagiosum.

Molluscum Contagiosum is a common infectious skin disease caused by a pox virus. It occurs predominantly in children and is characterised by the appearance on the body of lobulated epidermal outgrowths or lesions. These lesions, which are the result of excessive cellular proliferation stimulated in the keratinocyte layer by virus which has entered through the skin, appear as white shining papules, 5-10mm in diameter.

Each lesion, which may have a central pore, contains within its centre dead skin cells which have been killed by the virus.

Infections commonly last for 6-12 months but the condition can in certain cases persist for as long as 3-4 years. During this time, new crops of lesions appear, each lesion growing slowly for 6-12 weeks and persisting for an average of 3-4 months.

At present there is no drug treatment for Molluscum Contagiosum; the virus is resistant to the commonly used anti-viral agents which are effective in treating other viral infections and the disease is treated only by surgical removal of the lesions e.g. by cryotherapy. This can be painful and distressing, particularly for children, and does not of course prevent the reappearance of fresh lesions.

A need therefore exists for an improved method of treating Molluscum Contagiosum and particularly for a treatment which acts at the level of the underlying condition i.e. by combatting the infecting virus.

We have now surprisingly found that lithium is particularly useful in the treatment of Molluscum Contagiosum. In particular our studies have shown that lesions on infected individuals are reduced in number and eventually disappear upon topical application of lithium-containing preparations to the affected area, and that the treated area remains clear. In other words the reappearance of new lesions is prevented.

In one aspect the present invention therefore provides the use of a physiologically acceptable lithium compound, e.g. a water and/or lipid soluble lithium salt, in the manufacture of a medicament for use in the treatment and/or prophylaxis of Molluscum Contagiosum.

In a second aspect there is provided a method of treatment and/or prophylaxis of the human or animal body to combat Molluscum Contagiosum, said treatment comprising topically administering a physiologically acceptable lithium compound to affected areas on said body.

A third aspect of the invention provides use of a physiologically acceptable lithium compound for the treatment and/or prophylaxis of Molluscum Contagiosum.

In the medical field, lithium is known primarily for its therapeutic efficacy in a variety of mental and psychiatric disorders, most notably manic-depressive illness, but including also schizophrenia, alcoholism and certain dementias.

More recently lithium has been proposed for the treatment of Herpes infections and certain dermatitis skin conditions, as described for example in EP-A 013512 and EP-A 013126.

It is widely acknowledged however that lithium has toxic side effects and that the margin between therapeutic efficacy and toxicity is narrow. Indeed, it is usual to administer lithium only under close medical supervision.

Thus, in the absence of a strong positive indication of a beneficial activity against a given condition, lithium is not a drug which would be routinely administered as a matter of choice.

It was not therefore an obvious candidate in the search for a therapy for Molluscum Contagiosum. Moreover, its efficacy in this regard was both unpredictable and surprising; a positive effect on one viral infection cannot readily be extrapolated to a prediction of a similar effect on another. Thus, the efficacy of lithium in treating Herpes infections provided no expectation of a similar efficacy in treating Molluscum Contagiosum. This is borne out by observations that acyclovir, the most clinically effective drug in treating Herpes has no effect on Molluscum Contagiosum.

Lithium may be administered according to the invention in any form which will effectively deliver it to the virally infected area, although inorganic and organic salts are generally preferred. Suitable examples of organic and inorganic salts include lithium succinate, lithium chloride, lithium carbonate and lithium orotate, lithium succinate being generally preferred.

It may also be useful in certain circumstances to administer the lithium in the form of a salt with a polyunsaturated fatty acid, preferably a C₁₈₋₂₂ polyunsaturated fatty acid such as gammalinolenic or dihomogammalinolenic acid. This has the benefit that, being in a form which is both water and lipid soluble, the lithium is more effectively delivered across cell membranes, and at the same time can be easily formulated into aqueous-based non-greasy compositions.

Lithium is generally employed according to the present invention in the form of any pharmaceutical formulation suitable for topical administration. Thus for example, topical pharmaceutical compositions for use according to the present invention may be formulated in conventional manner as ointments, creams, lotions, gels, sprays, salves, sticks, soaps or any other appropriate vehicles. Thus, the chosen lithium compound may be

incorporated, optionally together with other active substances, with one or more conventional carriers, excipients or formulation aids. Suitable composition include for example those disclosed in EP-A-0289204 (Efamol Holdings PLC).

In a fourth aspect, the present invention therefore provides a topical pharmaceutical composition for use in the treatment and/or prophylaxis of *Molluscum Contagiosum*, said composition comprising a physiologically acceptable lithium compound together with at least one pharmaceutically acceptable carrier or excipient.

Benefits in lithium delivery may also be obtained by formulating the lithium with a skin penetration-assisting or keratolytic agent to aid transdermal passage of the lithium. Suitable keratolytic agents may be basic or acidic and include urea and salicylic acid. Suitable skin penetration-assisting agents include dimethylsulphacetamide or more preferably dimethylsulphoxide (DMSO).

Such pharmaceutical compositions comprising a physiologically acceptable lithium compound together with at least one keratolytic and/or skin-penetration-assisting agent and at least one pharmaceutically acceptable carrier or excipient form a fifth aspect of the invention.

The precise concentrations of lithium in the topical compositions of the invention will depend of course on a number of factors including for example, the severity of the condition to be treated, the form of lithium used and the physical nature of the pharmaceutical composition. Generally however an effective lithium concentration in the composition is 0.001 to 10% lithium ion, preferably 0.005 to 5%, and most especially preferably 0.3 to 2%.

The invention will now be described with reference to the following non-limiting examples in which all percentage, parts and ratios are by weight unless otherwise specified:

EXAMPLES

The Examples which follow illustrate the practice of this invention. In all cases the patients were treated twice daily with lithium succinate ointment (LSO) containing 8% lithium succinate in a wool alcohol ointment base.

Example 1

A four month old boy presented with 13 MC lesions on the trunk and arms: repeated crops of these lesions had appeared over the previous four months. LSO was applied twice daily to the lesions and to the surrounding skin. After six weeks there were only two lesions and after 12 weeks none.

Example 2

A four month old boy presented with severe MC with 55 lesions on the axillae, groins and legs. These were obviously causing him severe distress. Only 8 remained after six weeks treatment with LSO and all lesions were eliminated after 12 weeks.

Example 3

A 2 year old boy presented with MC. He had 16 lesions on various parts of the body. New lesions had been appearing over the previous two months. He was treated twice daily with LSO ointment. After 11 weeks only 6 lesions were left, after 17 weeks 3 lesions, and after 24 weeks the skin was completely clear.

Example 4

A seven year old girl with persistent MC which had lasted for over a year presented with 14 lesions. After 12 weeks only four lesions were left and after 24 weeks all lesions had disappeared.

Example 5

A five year old girl who had had persistent MC for over a year presented with 9 lesions on the buttocks. All lesions disappeared after treatment with LSO for 10 weeks.

The examples which follow illustrate pharmaceutical compositions according to the invention:

Example 6

A gel formulation comprising carbopol 934A (Goodrich) a gelling agent is prepared having the following composition:

5

Lithium succinate	7% by weight
Urea	10% by weight
Carbopol 934P	1% by weight
Dimethylsulphoxide (DMSO)	65% by weight
Triethanolamine - qs to pH	6.8% (approx. 0.15 ml)
Distilled water ad	100% by weight

10

15

A solution of lithium succinate in DMSO is prepared and is admixed with the remaining components in conventional manner.

20

Example 7

A gel composition comprising salicylic acid as the keratolytic agent is prepared with the following composition:

25

30

35

Lithium succinate	7% by weight
Salicylic acid	2% by weight
Klucel HF	2.5% by weight
Dimethylsulphoxide	65% by weight
Macrogol 300	18% by weight
Distilled water ad	100% by weight

Claims

1. Use of a physiologically acceptable lithium compound in the manufacture of a medicament for use in the treatment and/or prophylaxis of *Molluscum Contagiosum*.

2. Use as claimed in claim 1 of a water and/or lipid soluble lithium salt.

3. Use as claimed in claim 2 wherein the lithium salt is selected from lithium succinate, lithium chloride, lithium carbonate, lithium orotate and lithium salts of polyunsaturated fatty acids.

4. Use as claimed in claim 3 wherein said lithium salt is lithium gammalinolenate or lithium dihomogammalinolenate.

5. Use as claimed in any one of claims 1 to 4 for the manufacture of a medicament comprising 0.001 to 10% lithium ion.

6. Use as claimed in any one of claims 1 to 5 for the manufacture of a medicament comprising 0.3 to 2% lithium ion.

7. A pharmaceutical composition comprising a physiologically acceptable lithium compound together with at least one keratolytic and/or skin penetration assisting agent and at least one pharmaceutically acceptable carrier or excipient.

8. A composition as claimed in claim 7 wherein said keratolytic agent is selected from urea and salicylic acid.
9. A composition as claimed in claim 7 or claim 8 wherein said skin penetration-assisting agent is selected from dimethylsulphacetamide and dimethylsulphoxide.

5

10

15

20

25

30

35

40

45

50

55

THIS PAGE BLANK (USPTO)



Europäisches Patentamt

(19)

European Patent Office

Office européen des brevets



(11) Publication number : 0 484 112 A3

(12)

EUROPEAN PATENT APPLICATION

(21) Application number : 91309994.1

(22) Date of filing : 30.10.91

(51) Int. Cl.⁶ : A61K 33/00, A61K 31/20,
A61K 31/19, A61K 31/505,
A61K 33/14, A61K 47/20,
// (A61K33/00, 31:17, 31:60),
(A61K31/60, 31:19, 31:20,
31:505), (A61K33/14, 31:17,
31:60)

(30) Priority : 31.10.90 GB 9023701

(43) Date of publication of application :
06.05.92 Bulletin 92/19

(54) Designated Contracting States :
AT BE CH DE DK ES FR GB GR IT LI LU NL SE

(66) Date of deferred publication of search report :
08.07.92 Bulletin 92/28

(71) Applicant : EFAMOL HOLDINGS PLC
Efamol House Woodbridge Meadows
Guildford Surrey GU1 1BA (GB)

(72) Inventor : Horrobin, David Frederick
5n Maple Lodge, Lythe Hill Park
Haslemere, Surrey (GB)

(73) Representative : Cockbain, Julian, Dr. et al
Frank B. Dehn & Co. Imperial House 15-19,
Kingsway
London WC2B 6UZ (GB)

(64) Use of lithium in the treatment or prophylaxis of *Molluscum contagiosum*.

(67) The present invention provides use of a physiologically acceptable lithium compound in the manufacture of a medicament for use in the treatment and/or prophylaxis of *Molluscum Contagiosum*.

It also extends to pharmaceutical compositions comprising a physiologically acceptable lithium compound together with at least one keratolytic and/or skin penetration assisting agent and at least one pharmaceutically acceptable carrier or excipient.

EP 0 484 112 A3



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number

EP 91 30 9994

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Claims of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THIS APPLICATION (Int. CL.5)
A	EP-A-0 289 204 (EFAMOL) * Abstract; page 3, line 26 - page 4, line 18; page 4, lines 37-53; page 5, lines 21-34; examples 14,16,17 *	1-9	A 61 K 33/00 A 61 K 31/20 A 61 K 31/19 A 61 K 31/505
A	THE LANCET, vol. 2, no. 8344, 30th July 1983, page 288; G.R.B. SKINNER: "Lithium ointment for genital herpes" * Whole document *	1-9	A 61 K 33/14 A 61 K 47/20 // (A 61 K 33/00 A 61 K 31:17 A 61 K 31:60)
A	MEDICAL MICROBIOLOGY AND IMMUNOLOGY, vol. 168, 1980, pages 139-148, Springer-Verlag; G.R.B. SKINNER et al.: "The effect of lithium chloride on the replication of Herpes simplex virus" * Whole document *	1-9	(A 61 K 31/60 A 61 K 31:19 A 61 K 31:20 A 61 K 31:505) (A 61 K 33/14 A 61 K 31:17 A 61 K 31:60)
A	B.N. FIELDS et al.: "Fields Virology", vol. 2, 2nd edition, 1990, pages 2130-2131: "Molluscum contagiosum", Raven Press, New York, US * Whole document *	1-9	
A	D.O. WHITE et al.: "Medical Virology", 3rd edition, 1986, pages 433-443: "Poxviruses", Academic Press, London, GB * Whole document *	1-9	
A	R. BERKOW et al.: "The Merck Manual of Diagnoses and Therapy", 15th edition, 1987, pages 2274-2277: "Viral infections of the skin", Merck & Co., Inc., Rahway, N.J., US * Whole document *	1-9	
<p>The present search report has been drawn up for all claims</p> <p>Date of completion of the search</p> <p>SEARCHER</p>			
Place of search	07-04-1992	GOETZ G.	
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : see-written disclosure P : intermediate document			
T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons A : member of the same patent family, corresponding document			



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) Publication number:

0 520 112 A1

(12)

EUROPEAN PATENT APPLICATION

(21) Application number: 91401785.0

(51) Int. Cl.5: A61K 7/48, A61K 7/06,
A61K 7/16

(22) Date of filing: 28.06.91

(43) Date of publication of application:
30.12.92 Bulletin 92/53

(71) Applicant: JAPAN FINE CHEMICAL CO., LTD.
186-3, Higashihatsuishi 2-chome
Nagareyama-shi, Chiba-ken(JP)

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LI LU NL SE

(72) Inventor: Yamada, Hajime
186-3, Higashihatsuishi 2-chome
Nagareyama-shi, Chiba-ken(JP)
Inventor: Yamada, Akira
186-3, Higashihatsuishi 2-chome
Nagareyama-shi, Chiba-ken(JP)

(74) Representative: Gillard, Marie-Louise et al
Cabinet Beau de Loménie 55, Rue
d'Amsterdam
F-75008 Paris(FR)

(54) Dermatological composition based on an aqueous phase.

(57) The present invention relates to a dermatological composition composed for cosmetics or medicines for external application to skin and to oral or nasal mucous-membrane. This composition can be applied in particular in the cosmetic or pharmaceutical field, especially in the dermatological cases to regenerate and to revitalize damaged cells by equilibrating electrochemical ion gradients across cell membrane and also by osmotic pressure on the inner face of the cell membrane. A composition based on a water phase in accordance with present invention comprises dextran, glucose, mutan, NaCl, KCl, and CaCl₂, which are dissolved in the aqueous phase.

EP U 520 112 A1

[Background of the Invention]

The present invention relates to a dermatological composition composed for external application to skin and to oral or nasal mucous-membrane. This composition can be applied in particular in the cosmetic or pharmaceutical field, especially in the dermatological cases to regenerate and to revitalize damaged cells by equilibrating electrochemical ion gradients across cell membrane and also by osmotic pressure on the inner face of the cell membrane. The osmotic pressure thereon is counterbalanced by osmotic pressure exerted by the molecules chiefly Na and Cl in the extracellular fluid.

In recent years, there has been remarkable advances in developing cosmetic or pharmaceutical compositions, especially dermatological compositions used for external application to skin or mucous membrane, and various kinds of such compositions were developed which contribute to be treatment of some of the skin disorders. Most of these conventional compositions are dispensed in the form of liquid, for example face lotion, or in the form of cream, ointment or the like, by mixing an essential composition with a base material such as methyl cellulose, synthetic-resin emulsion, polyethylene glycol, powder or the like.

Furthermore there has been a demand for a dermatological composition as a barrier for protecting the surface of skin from drying, wetting, exposuring to glaring sunlight or ultraviolet light, or other environmental factors.

All living cells and their cell-organelle are protected from their surroundings by biological membranes having selective permeabilities against simple ions, sugars and the like. The selective permeabilities of biological membranes, for example the permeability to simple ions such as Na and K, creates large differences in the ionic composition of the cell-interior compared to the extracellular fluid, and thus this enables cell membranes to store potential energy in the form of ion gradients which can be obserbed by the membrane potential. Therefore the transmembrane ion gradients make ATPs (adenosine 5'-triphosphates) which are responsible to drive various transport processes and to transmit electrical signals across the membrane.

Furthermore, the membrane potential that exists across the cell membrane is maintained by a Na-K pump which generates K and Na concentration gradients in opposite directions of the membrane. The Na-K pump links with the Na-K ATPase which helps not only maintaining of the electrical potential across the membrane but also regulating of the cell volume. The Na-K ATPase controls the solute concentrations inside the cell and thereby the osmotic forces that would tend to make the cell swell or shrink.

But for the most cells of multicellular animals, the Na-K ATPase is crucial, so that the cell for example a human blood-cell or a bacterial cell can be shranked when it exposed to hypertonic solution. In contrast, the cell can be swollen or lysed when it exposed to hypotonic solution. Thus the solute concentration of the extracellular space should be regulated.

Accordingly, when the surface of skin is damaged by the above mentioned factors, the equilibrium of the ionic gradients across cell membrane of the skin can be destroyed. For restoring the ionic equilibrium state across the membrane, an appropriate ionic composition should be applied to the extracellular space.

It is known that NaCl shows an important role for maintaining the above described equilibrium between the inside (cytoplasm) and the outside (extracellular space) of the cell.

In the case of a human body fluid, for example, 0.9% NaCl solution is isotonic with the extracellular fluid and thus it is used as an isotonic sodium chloride solution or a physiological saline in the medical field.

In an animal body, glucose is usually converted into glycogen and stored in liver or muscle as an energy source or nutrition source for the vital cells, and also glucose is usually lysed in the process known as glycolysis. In this process, a glucose molecule with six carbon atoms is converted into two small molecules of pyruvate which enters the mitochondria to be completely oxidized to CO₂ and H₂O and to generate ATP required for many biosyntheses. Accordingly, it has been known that glucose is the principal food compound of many cells. In the course of glucose breakdown as described above, energy is produced and used to drive biosynthetic reactions and to other energy-requiring processes in the cell. Therefore, it is preferable to administrate glucose in the form of a liquid to an animal by oral, intravenous, or intramuscular administration.

In the case of blood plasma which is easily isolated from an animal body, it has been known that the blood plasma permeates through skin and mucous membrane and thus it plays an essential role in the skin-restoration processes when it is applied on the surface of skin. Accordingly, the isolated-plasma is used as an ingredient of a medicine for external application.

To protect the skin from the above described injurious factor, some of the conventional cosmetics or medicines comprise an inorganic salt such as sodium chloride, glucose or one of the other natural sugars, or a blood plasma fraction.

In the document of U.S. Patent No. 3574854, for example, a dermatological composition in the form of

cream has been disclosed. This composition comprises NaCl as an ingredient for restoring the damaged skin to be soft to the touch. Also the document of German Patent Application No. 3327840 discloses a dermatological composition comprising a mineral salt as an ingredient for sterilizing or disinfecting the surface of skin from the bacterial contamination. Furthermore U.S. patent No. 3859436 discloses a

- 5 dermatological composition comprising glucose as an ingredient for smoothing the surface of skin, and in addition U.S. Patent No. 3777597 discloses a dextran solution for a shaving lotion or the like.

Accordingly, these conventional dermatological compositions have been used as cosmetics or medicines for external application to protect the surface of skin from the above described injurious factors.

- As described above, the conventional dermatological compositions have been recognized as biological 10 components for maintaining physiological functions of cell. However, the conventional dermatological composition shows several disadvantages:

- (1) in the case of a dermatological composition comprising NaCl for killing bacteria or the like, water can be lost from the skin cell having excess of sodium;
- (2) in the case of a dermatological composition comprising glucose or an other natural sugar, topically-applied glucose cannot be breakdown into simple substances because glucose is not absorbed from the 15 surface of skin; and
- (3) in the case of a dermatological composition comprising blood plasma isolated from human or animal body, the isolated-plasma is easily denatured and thus it must be mixed with polyethylene glycol as a protecting agent when it is used as an ingredient of the medicine (remarkably, polyethylene glycol must be included in at least more than 60% of a total weight of the medicine to protect proteins such as 20 serum protein, coagulation proteins and the like contained in the plasma).

Accordingly, the conventional compositions as described above are difficult to comprise in a medicine for external application for restoring physiological disorders of skin cells. In addition, the conventional compositions as described above are unsuitable for treating some of the dermatological diseases such as 25 athlete's foot, offensive smell of the armpit, baldness, scurf, itching, or the like, which are caused by inhibiting blood circulation in capillary vessel in the skin and by arresting cell division of the skin cells.

To solve the above problems, we found the dermatological composition as disclosed in Japanese Patent Application (TOKKAISHO 61-24630). It discloses a dermatological composition which is responsible for recovering physiological functions of damaged skin by equilibrating electropotential ion gradients and 30 osmotic forces across cell membrane. In addition, this composition facilitates the cell division and shows preferable effects on restoring pigmentation and erubescence face. Thus the dermatological composition according to the above reference can be comprised in lotion and shows regenerating or revitalizing activity to the skin when it is applied on face, hand, hair or the other regions except mucous membrane.

35 [Summary of the Invention]

It is therefore a principal object of the present invention to provide a composition used for cosmetics or medicine for external application to mucous membrane for restoring or improving dermatological symptoms such as stomatitis, pollinosis or the like.

40 So as to achieve the above described object, the present invention provides a composition comprising dextran, glucose, mutan, lenthynan, NaCl, KCl, and CaCl₂, dissolved in an aqueous phase. Concentration of these ingredients of the composition is as follows: each concentration of dextran, glucose, mutan, and lenthynan is between 5 to 30% of the weight of said composition, respectively, and each concentration of NaCl, KCl, and CaCl₂ is between 0.1 to 1% of the weight of said composition, respectively.

45 In the present invention, the percentages are given by weight, unless indicated otherwise.

Mutan, lenthynan and dextran used in the invention composition are polysaccharides, characterized as follows:

50 (1) Dextran is an alpha-1, 6-glucan which is produced from sucrose by one of the lactate bacteria such as Leuconostoc mesenteroides and is used as a plasma expander (a plasma substitute).

Dextran has a linear chain consisting of a plurality of D-glucopyranose units which are linked with each other by alpha (1 - 6) bonding and branched chains which are linked with position 3 or 4 of the linear chain.

(2) Mutan is an insoluble and cohesive molecule of an alpha-1, 3-1, 6-glucan.

Mutan is produced from sucrose by Streptococcus mutans and is responsible for decaying teeth.

55 (3) Lenthynan is a beta-1, 3-1, 6-glucan which is produced by Lentinus edodes and it has immunological properties such as action of macrophage.

Other objects, characteristics and advantages of the invention will become more clearly apparent from the following explanatory description referring to the following example, which cannot in any way limit the

scope of the invention.

[Description of the Preferred Embodiments]

5 A composition in accordance with a preferred embodiment of the present invention comprises dextran, glucose, mutan, lenthynan, NaCl, KCl, and CaCl₂, dissolved in an aqueous phase. Concentration of these ingredients of the composition is as follows: each concentration of dextran, glucose, mutan, and lenthynan is between 5 to 30% of the weight of said composition, respectively, and each concentration of NaCl, KCl, and CaCl₂ is between 0.1 to 1% of the weight of said composition, respectively.

10 It is preferable in these compositions according to the present invention, the above described ingredients are dissolved in an aqueous phase at a temperature of between 50 to 100°C and the aqueous phase should be a pure water which does not contain any oily material such as a detergent or the like.

In accordance with the preferred embodiments of the present invention, a cosmetic or pharmaceutical substance, especially dermatological substance comprises a composition based on an aqueous phase, 15 wherein dextran, glucose, mutan, and lenthynan is dissolved in the aqueous phase.

It is preferable that the above described composition based on an aqueous phase further comprises NaCl, KCl, and CaCl₂. In this composition, these ingredients are dissolved in the aqueous phase.

In accordance with another preferred embodiment of the present invention, a cosmetic or pharmaceutical substance, especially dermatological substance, wherein dextran, glucose, mutan, lenthynan, NaCl, KCl, and 20 CaCl₂ dissolved in the aqueous phase and each concentration of these ingredients is as follows: each concentration of dextran, glucose, mutan, and lenthynan is between 5 to 30% of the weight of the composition, respectively, and each concentration of NaCl, KCl, and CaCl₂ is between 0.1 to 1% of the weight of the composition, respectively.

It is preferable in these cosmetic or pharmaceutical substances according to the present invention, the 25 above described ingredients are dissolved in the aqueous phase at a temperature of between 50 to 100°C and the aqueous phase should be a pure water which does not contain any oily material such as a detergent or the like.

[Example]

30 Table 1 shows a composition in accordance with a preferred embodiment of the present invention. These ingredients shown in the table 1 were dissolved in a distilled water at 50-100°C.

An obtained composition is used as a medicine for external application. The efficiencies of the composition against various kinds of skin disorders were assayed as follows.

35 540 patients suffered from one of the skin disorders were grouped into each corresponding symptom as described in table 2.

A suitable amount of the above described composition was administrated to each patient for 6 months and after that the efficiencies of the composition were estimated as follows. A patient who did not show any improvement of the symptom made no point of efficiency: a patient who showed any improvement of the 40 symptom made one point of efficiency: and a patient who was cured of disease made 2 points of efficiency. These individual points were summed up in each symptom and then the sum of the points were listed in table 2.

In addition, an efficiency was indicated by a rate value calculated by following formula in each symptom.

45 Efficiency (%) = a total of points/ a total of patient X 2 x 100

50

55

Table 1

An amount of each ingredient of a composition according to the present invention.		
	ingredients	% by weight of a composition
5	dextran	20
10	glucose	10
15	mutan	10
	lenthynan	10
	NaCl	0.9
	CaCl ₂	0.3
	KCl	0.3
	Distilled water	48.5
20	total	100.0

Table 2

The efficiencies of the composition against different symptoms.				
	symptoms	No. of patients	points	efficiency (%)
25	male pattern baldness	60	118	98
	nervous baldness	50	50	50
30	pimples	30	56	93
	erubescence face	60	64	53
	athlete's foot	50	94	93
	seborrheic dermatosis	100	196	98
	atopic dermatosis	100	94	47
	stomatitis	50	100	100
	allergic rhinitis	40	80	100

35 It has been known that some of skin diseases listed in Table 2 are difficult to treat or to improve their conditions by topical application of the conventional composition.

As shown in Table 2, however, the novel composition according to the present invention is able to improve these conditions, and especially in the cases of stomatitis and allergic rhinitis, 100% efficiency is obtained.

40 From the results of the above described assay, the present invention provides a composition which is able to equilibrate electrochemical ion gradients and osmotic forces across mucous membrane. Accordingly, the oral and nasal mucous membranes are not stimulated by the present composition and thus stomatitis and allergic rhinitis is cured at 100% efficiency.

45 While the described embodiment represents the preferred form of the present invention, it is to be understood that modifications will occur to those skilled in that art without departing from the spirit of the invention. The scope of the invention is therefore to be determined solely by the appended claims.

Claims

- 50 1. A composition based on an aqueous phase comprising lenthynan, dextran, glucose, mutan, NaCl, KCl and CaCl₂ which are dissolved in said aqueous phase.
- 55 2. A composition in accordance with claim 1, wherein each concentration of dextran, glucose, mutan, and lenthynan is between 5 to 30% of the weight of said water phase respectively, and each concentration of NaCl, KCl, and CaCl₂ is between 0.1 to 1% of the weight of said water phase respectively.
- 55 3. A composition according to claim 1 or 2, wherein dextran, glucose, mutan, lenthynan, NaCl, KCl, and CaCl₂ are dissolved in said water phase at a temperature of between 50 to 100°C.

4. A composition according to any one of claims 1 to 3, wherein said water phase is a pure water which does not contain any oily material.
5. A cosmetic or pharmaceutical substance, especially dermatological substance, which comprises a composition according to any one of claims 1 to 4.

10

15

20

25

30

35

40

45

50

55



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number

EP 91 40 1785

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citations of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. 5)
A	WPIL, FILE SUPPLIER, AN=86-329438, Derwent Publications Ltd, London, GB; & JP-A-61 246 130 (JAPAN FINE CHEM. K.K.) 01-11-1986 * Whole abstract * -----	1,2	A 61 K 7/48 A 61 K 7/06 A 61 K 7/16
			TECHNICAL FIELDS SEARCHED (Int. Cl. 5)
			A 61 K
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
THE HAGUE	25-11-1991	COUCKUYT P.J.R.	
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

This Page Blank (uspto)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.

This Page Blank (uspto)